IN THE CLAIMS

The status of each claim is listed below.

Claims 1-85: (Canceled).

86. (Previously Presented): A method for providing bacterial or yeast cells with the capacity to produce a protein, the amino acid sequence of which comprises at least one unconventional amino acid, comprising:

(a) introducing at least one missense mutation in a target codon of a gene encoding a protein required for the growth of the bacterial or yeast cells, wherein the mutated protein synthesized from the mutated gene is not functional in the bacterial or yeast cells; and

(b) selecting the bacterial or yeast cells obtained in (a) in a culture medium which (1) does not contain a nutrient compensating for the loss of functionality of the mutated protein and (2) contains an unconventional amino acid which restores the functionality of said protein required for growth of the bacterial or yeast cells, said unconventional amino acid being that encoded by said target codon; and

(c) culturing the bacterial or yeast cells obtained in (b) in a culture medium containing said amino acid encoded by said target codon.

87. (Previously Presented): The method of Claim 86, further comprising an additional culturing in a culture medium containing a nutrient compensating for the loss of functionality of the mutated protein.

88. (Previously Presented): The method according to Claim 86, wherein the step of culturing the cells comprises a series of cultivation steps of the same cells under selective

conditions until mutants capable of growing in the absence of the nutrient required by loss of the functionality of the mutated protein are obtained.

89. (Previously Presented): The method of Claim 86, wherein the missense mutation is chosen from missense mutations which spontaneously reverse at a frequency of one organism from at least 10^{15}.

90. (Currently Amended): The method of Claim 86, wherein the missense mutation transforms a target codon of a gene encoding a protein required for the growth of said cell ~~ecll,~~ into a codon, which, in comparison with the target codon, exhibits a change of at least two bases.

91. (Previously Presented): The method of Claim 86, wherein the target codon encodes an amphiphilic amino acid.

92. (Previously Presented): The method of Claim 86, wherein the target codon encodes an amino acid which has a steric volume which is the same as or smaller than the steric volume of the amino acid encoded by the missense mutation.

93. (Previously Presented): The method of Claim 90, wherein the target codon encodes cysteine.

94. (Previously Presented): The method of Claim 90, wherein the amino acid encoded by the missense mutation is valine or isoleucine.

95. (Previously Presented): The method of Claim 86, wherein said introducing is carried out using a vector comprising the mutated sequence of said gene encoding a protein required for the growth of said cells, including said missense mutation.

96. (Previously Presented): The method of Claim 95, wherein said vector is a plasmid vector.

97. (Previously Presented): The method of Claim 86, further comprising isolating the cells which grow in said culturing of c).

98. (Previously Presented): Method of Claim 97, further comprising culturing the isolated cells in a second culture medium containing said amino acid encoded by said target codon.

99. (Previously Presented): The method of Claim 98, wherein the concentration of said amino acid in said second culture medium is at a concentration higher than the concentration of said amino acid in said first culture medium, and wherein the method further comprises selecting the cells sensitive to the concentration of said amino acid in said second culture medium.

100. (Previously Presented): The method of Claim 97, wherein an aminoacyl-tRNA synthetase which recognizes the amino acid encoded by said missense mutation of said selected cells is capable of charging onto one of its associated tRNAs an unconventional amino acid or an amino acid other than said amino acid encoded by said missense mutation.

101. (Previously Presented): The method of Claim 100, wherein the nucleic acid sequence of the gene encoding said aminoacyl-tRNA synthetase includes at least one mutation compared with the sequence of the corresponding wild-type gene.

102. (Previously Presented): The method of Claim 101, wherein said mutation in the nucleic acid sequence of the gene encoding said aminoacyl-tRNA synthetase is generated in vivo.

103. (Currently Amended): A bacterial or yeast cell, ~~obtained~~ obtainable by the method of Claim 86, ~~capable of producing a protein, wherein the amino acid sequence of the protein is mutated by comprising at least one unconventional amino acid, wherein the cell comprises a valyl-tRNA synthetase which recognizes a given amino acid and which is capable of charging onto one of its associated tRNAs an unconventional amino acid or an amino acid other than said given amino acid, and in that the nucleic acid sequence of the gene encoding said valyl-tRNA synthetase includes at least one mutation compared with the sequence of the wild-type valyl-tRNA gene~~ wherein said cell comprises valyl-tRNA synthase including at least one mutation corresponding to K277Q, R223H, V276A or D230N, which allows said valyl-tRNA synthase to charge compounds that show steric resemblance to valine.

104. (Previously Presented): The isolated cell of Claim 103, which is an *E. coli* strain.

Claim 105: (Canceled).

106. (Currently Amended): The isolated cell of Claim 103, which is selected from the group consisting of the following cells deposited at the CNCM (Collection Nationale de Culture de Microorganismes [National Collection of Microorganism Cultures], Paris, France):

(a) *E. coli* strain deposited at the CNCM under the No. I-2026 on May 25, 1998,

(b) *E. coli* strain deposited at the CNCM under the No. I-2027 on May 25, 1998,

(c) *E. coli* strain deposited at the CNCM under the No. I-2339 on October ~~October~~ 26, 1999,

(d) *E. coli* strain deposited at the CNCM under the No. I-2340 on October 26, 1999, and

(e) *E. coli* strain deposited at the CNCM under the No. I-2341 on October 26, 1999.

107. (Previously Presented): A method of producing a protein the amino acid sequence of which comprises at least one unconventional amino acid, comprising culturing the isolated cell of Claim 103 under conditions to produce the protein.

108. (Previously Presented): A process for producing a protein the amino acid sequence of which comprises at least one unconventional amino acid, comprising:

(a) selecting a cell by the method according to Claim 97;

(b) growing said cell selected in (a) in a culture medium comprising at least one unconventional amino acid or a precursor thereof and under culture conditions which allow the growth of said cell, and

(c) producing a supernatant or a cell pellet from the cell culture; and

(d) isolating from the culture supernatant and/or from the cell pellet produced in step (c) a protein comprising said unconventional amino acid.

109. (Currently Amended): The process of Claim 108~~,~~ wherein cell ~~said~~ culture medium in (b), which allows the growth of said cell, contains a precursor of said unconventional amino acid.

110. (Previously Presented): The process of Claim 108, wherein said unconventional amino acid is synthesized by said cell.

111. (Previously Presented): The process of Claim 110, wherein the synthesis of said unconventional amino acid is increased by genetic modification of said cell.

112. (Previously Presented): The process of Claim 108, wherein said cell is auxotrophic for the amino acid encoded by said target codon.

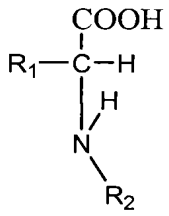
113. (Previously Presented): The process of Claim 108, wherein said cell comprises a homologous or heterologous gene of interest the coding sequence of which includes at least one target codon.

114. (Previously Presented): The process of Claim 113, wherein the culture medium for growing cells in (b) further comprises the compounds required for inducing the synthesis of the protein encoded by said gene of interest.

115. (Previously Presented): The process of Claim 113, wherein the biological activity of the protein encoded by said gene of interest is at least partially conserved after the

incorporation of said unconventional amino acid at the level of the target codon of said gene of interest.

116. (Previously Presented): The process of Claim 108, wherein one of the unconventional amino acids present in the culture medium for growing cells in step (b) is represented by an amino acid of formula I having L configuration:



(I)

wherein R_1 or R_2 represents radicals containing a functional group capable of reacting selectively.

117. (Previously Presented): The process of Claim 116, wherein the functional group is selected from the group consisting of aldehyde, ketone, ethenyl, ethynyl, and nitrile groups.

118. (Previously Presented): A process for functionalization of a protein comprising incorporating into the amino acid sequence of said protein an unconventional amino acid containing a functional group, wherein said incorporation is done according to the process of Claim 108.

119. (New) The bacterial or yeast cell of Claim 103, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to K277Q.

120. (New) The bacterial or yeast cell of Claim 103, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to R223H.

121. (New) The bacterial or yeast cell of Claim 103, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to V276A.

122. (New) The bacterial or yeast cell of Claim 103, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to D230N.

123. (New) The bacterial or yeast cell of Claim 103, wherein the compounds that show steric resemblance to valine are selected from the groups consisting of cystein, L-2-aminobutyrate, L-2-aminovalerate, L-2-3-diaminopropionate and L-3-thiol-2-aminobutyrate.

124. (New) The bacterial or yeast cell of Claim 103, which is obtained by said method.

125. (New) A bacterial or yeast cell, which comprises valyl-tRNA synthase including at least one mutation corresponding to K277Q, R223H, V276A or D230N, which allows said valyl-tRNA synthase to charge compounds that show steric resemblance to valine..

126. (New) The bacterial or yeast cell of Claim 125, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to K277Q.

127. (New) The bacterial or yeast cell of Claim 125, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to R223H.

128. (New) The bacterial or yeast cell of Claim 125, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to V276A.

129. (New) The bacterial or yeast cell of Claim 125, wherein said cell comprises valyl-tRNA synthase including a mutation corresponding to D230N.

130. (New) The bacterial or yeast cell of Claim 125, wherein the compounds that show steric resemblance to valine are selected from the groups consisting of cystein, L-2-aminobutyrate, L-2-aminovalerate, L-2-3-diaminopropionate and L-3-thiol-2-aminobutyrate.

131. (New) The bacterial or yeast cell of Claim 103, wherein said compounds that show steric resemblance to valine is cystein.

132. (New) The bacterial or yeast cell of Claim 125, wherein said compounds that show steric resemblance to valine is cystein.

133. (New) The bacterial or yeast cell of Claim 103, wherein the yeast is *Saccharomyces cerevisiae*.

134. (New) The bacterial or yeast cell of Claim 125, wherein wherein the yeast is *Saccharomyces cerevisiae*.